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CONTENTS/SUMMARIES

Summary: Complex retroviruses are distinguished by their ability to control the expression of their gene products through the action of virally encoded regulatory proteins. These viral gene products modulate both the quantity and the quality of viral gene expression through regulation at both the transcriptional and posttranscriptional levels. The most intensely studied retroviral regulatory proteins, termed Tat and Rev, are encoded by the prototypic complex retrovirus human immunodeficiency virus type 1. However, considerable information also exists on regulatory proteins encoded by human T-cell leukemia virus type I, as well as several other human and animal complex retroviruses. In general, these data demonstrate that retrovirally encoded transcriptional trans-activators can exert a similar effect by several very different mechanisms. In contrast, posttranscriptional regulation of retroviral gene expression appears to occur via a single pathway that is probably dependent on the recruitment of a highly conserved cellular cofactor. These two shared regulatory pathways are proposed to be critical to the ability of complex retroviruses to establish chronic infections in the face of an ongoing host immune response.

Summary: The outer membrane of gram-negative bacteria provides the cell with an effective permeability barrier against external noxious agents, including antibiotics, but is itself a target for antibacterial agents such as polycations and chelators. Both groups of agents weaken the molecular interactions of the lipopolysaccharide constituent of the outer membrane. Various polycations are able, at least under certain conditions, to bind to the anionic sites of lipopolysaccharide. Many of these disorganize and cross the outer membrane and render it permeable to drugs which permeate the intact membrane very poorly. These polycations include polymyxins and their derivatives, protamine, polymers of basic amino acids, compound 48/80, insect cecropins, reptilian magainins, various cationic leukocyte peptides (defensins, bactenecins, bactericidal/permeability-increasing protein, and others), aminoglycosides, and many more. However, the cationic character is not the sole determinant required for the permeabilizing activity, and therefore some of the agents are much more effective permeabilizers than others. They are useful tools in studies in which the poor permeability of the outer membrane poses problems. Some of them undoubtedly have a role as natural antibiotic substances, and they or their derivatives might have some potential as pharmaceutical agents in antibacterial therapy as well. Also, chelators (such as EDTA, nitrilotriacetic

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acid, and sodium hexametaphosphate), which disintegrate the outer membrane by removing Mg^{2+} and Ca^{2+}, are effective and valuable permeabilizers.

Summary: All living cells must conduct protein synthesis with a high degree of accuracy maintained in the transmission and flow of information from gene to finished protein product. One crucial "quality control" point in maintaining a high level of accuracy is the selectivity by which aminoacyl-tRNA synthetases furnish correctly activated amino acids, attached to tRNA species, as the building blocks for growing protein chains. During selection of amino acids, synthetases very often have to distinguish the cognate substrate from a homolog having just one fewer methyl group in its structure. The binding energy of a methyl group is estimated to contribute only a factor of 100 to the specificity of binding, yet synthetases distinguish such closely related amino acids with a discrimination factor of 10,000 to 100,000. Examples of this include methionine versus homocysteine, isoleucine versus valine, alanine versus glycine, and threonine versus serine. Many investigators have demonstrated in vitro the ability of certain aminoacyl-tRNA synthetases to edit, that is, correct or prevent incorrect attachment of amino acids to tRNA molecules. Several major editing pathways are now established from in vitro data. Further, at least some aminoacyl-tRNA synthetases have recently been shown to carry out the editing function in vivo. Editing has been demonstrated to occur in both Escherichia coli and Saccharomyces cerevisiae. Significant energy is expended by the cell for editing of misactivated amino acids, which can be reflected in the growth rate. Because of this, cellular levels of aminoacyl-tRNA synthetases, as well as amino acid biosynthetic pathways which yield competing substrates for protein synthesis, must be carefully regulated to prevent excessive editing. High-level expression of recombinant proteins imposes a strain on the biosynthetic capacity of the cell which frequently results in misincorporation of abnormal or wrong amino acids owing in part to limited editing by synthetases. Unbalanced amino acid pools associated with some genetic disorders in humans may also lead to errors in tRNA aminoacylation. The availability of X-ray crystallographic structures of some synthetases, combined with site-directed mutagenesis, allows insights into molecular details of the extraordinary selectivity of synthetases, including the editing function.

Bacteriophage lysis involves at least two fundamentally different strategies. Most phages elaborate at least two proteins, one of which is a murein hydrolase, or lysin, and the other is a membrane protein, which is given the designation holin in this review. The function of the holin is to create a lesion in the cytoplasmic membrane through which the murein hydrolase passes to gain access to the murein layer. This is necessary because phage-encoded lysins never have secretory signal sequences and are thus incapable of unassisted escape from the cytoplasm. The holins, whose prototype is the λ S protein, share a common organization in terms of the arrangement of charged and hydrophobic residues, and they may all contain at least two transmembrane helical domains. The available evidence suggests that holins oligomerize to form nonspecific holes and that this hole-forming step is the regulated step in phage lysis. The correct scheduling of the lysis event is as much an essential feature of holin function as is the hole formation itself. In the second strategy of lysis, used by the small single-stranded DNA phage φX174 and the single-stranded RNA phage MS2, no murein hydrolase activity is synthesized. Instead, there is a single species of small membrane protein, unlike the holins in primary structure, which somehow causes disruption of the envelope. These lysis proteins function by activation of cellular autolysins. A host locus is required for the lytic function of the φX174 lysis gene E.

Summary: A wide variety of compounds can be biodegraded via reductive removal of halogen substituents. This process can degrade toxic pollutants, some of which are not

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known to be biodegraded by any other means. Reductive dehalogenation of aromatic compounds has been found primarily in undefined, syntrophic anaerobic communities. We discuss ecological and physiological principles which appear to be important in these communities and evaluate how widely applicable these principles are. Anaerobic communities that catalyze reductive dehalogenation appear to differ in many respects. A large number of pure cultures which catalyze reductive dehalogenation of aliphatic compounds are known, in contrast to only a few organisms which catalyze reductive dehalogenation of aromatic compounds. Desulfomonile tiedjei DCB-1 is an anaerobe which dehalogenates aromatic compounds and is physiologically and morphologically unusual in a number of respects, including the ability to exploit reductive dehalogenation for energy metabolism. When possible, we use D. tiedjei as a model to understand dehalogenating organisms in the above-mentioned undefined systems. Aerobes use reductive dehalogenation for substrates which are resistant to known mechanisms of oxidative attack. Reductive dehalogenation, especially of aliphatic compounds, has recently been found in cell-free systems. These systems give us an insight into how and why microorganisms catalyze this activity. In some cases transition metal complexes serve as catalysts, whereas in other cases, particularly with aromatic substrates, the catalysts appear to be enzymes.